

SEQUENCE LISTING

<110> Hopf, Carsten
Drewes, Gerard
Ruffner, Heinz

<120> Treatment of Neurodegenerative Diseases by the Use of GPR49

<130> 50125/113001

<140> US 10/587,159

<141> 2006-07-25

<150> PCT/EP2004/013539

<151> 2004-11-29

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<150> EP 04007447.8

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<151> 2004-01-29

<160> 4

<170> PatentIn version 3.3

<210> 1

<211> 21

<212> DNA

<213> Artificial sequence

<220>

<223> designed siRNA

<400> 1

aacagcagta tggacgacct t

21

<210> 2

<211> 907

<212> PRT

<213> Homo sapiens

<400> 2

Met Asp Thr Ser Arg Leu Gly Val Leu Leu Ser Leu Pro Val Leu Leu

1

5

10

15

Gln Leu Ala Thr Gly Gly Ser Ser Pro Arg Ser Gly Val Leu Leu Arg
 20 25 30

Gly Cys Pro Thr His Cys His Cys Glu Pro Asp Gly Arg Met Leu Leu
 35 40 45

Arg Val Asp Cys Ser Asp Leu Gly Leu Ser Glu Leu Pro Ser Asn Leu
 50 55 60

Ser Val Phe Thr Ser Tyr Leu Asp Leu Ser Met Asn Asn Ile Ser Gln
 65 70 75 80

Leu Leu Pro Asn Pro Leu Pro Ser Leu Arg Phe Leu Glu Glu Leu Arg
 85 90 95

Leu Ala Gly Asn Ala Leu Thr Tyr Ile Pro Lys Gly Ala Phe Thr Gly
 100 105 110

Leu Tyr Ser Leu Lys Val Leu Met Leu Gln Asn Asn Gln Leu Arg His
 115 120 125

Val Pro Thr Glu Ala Leu Gln Asn Leu Arg Ser Leu Gln Ser Leu Arg
 130 135 140

Leu Asp Ala Asn His Ile Ser Tyr Val Pro Pro Ser Cys Phe Ser Gly
 145 150 155 160

Leu His Ser Leu Arg His Leu Trp Leu Asp Asp Asn Ala Leu Thr Glu
 165 170 175

Ile Pro Val Gln Ala Phe Arg Ser Leu Ser Ala Leu Gln Ala Met Thr
 180 185 190

Leu Ala Leu Asn Lys Ile His His Ile Pro Asp Tyr Ala Phe Gly Asn
 195 200 205

Leu Ser Ser Leu Val Val Leu His Leu His Asn Asn Arg Ile His Ser
 210 215 220

Leu Gly Lys Lys Cys Phe Asp Gly Leu His Ser Leu Glu Thr Leu Asp
 225 230 235 240

Leu Asn Tyr Asn Asn Leu Asp Glu Phe Pro Thr Ala Ile Arg Thr Leu
245 250 255

Ser Asn Leu Lys Glu Leu Gly Phe His Ser Asn Asn Ile Arg Ser Ile
260 265 270

Pro Glu Lys Ala Phe Val Gly Asn Pro Ser Leu Ile Thr Ile His Phe
275 280 285

Tyr Asp Asn Pro Ile Gln Phe Val Gly Arg Ser Ala Phe Gln His Leu
290 295 300

Pro Glu Leu Arg Thr Leu Thr Leu Asn Gly Ala Ser Gln Ile Thr Glu
305 310 315 320

Phe Pro Asp Leu Thr Gly Thr Ala Asn Leu Glu Ser Leu Thr Leu Thr
325 330 335

Gly Ala Gln Ile Ser Ser Leu Pro Gln Thr Val Cys Asn Gln Leu Pro
340 345 350

Asn Leu Gln Val Leu Asp Leu Ser Tyr Asn Leu Leu Glu Asp Leu Pro
355 360 365

Ser Phe Ser Val Cys Gln Lys Leu Gln Lys Ile Asp Leu Arg His Asn
370 375 380

Glu Ile Tyr Glu Ile Lys Val Asp Thr Phe Gln Gln Leu Leu Ser Leu
385 390 395 400

Arg Ser Leu Asn Leu Ala Trp Asn Lys Ile Ala Ile Ile His Pro Asn
405 410 415

Ala Phe Ser Thr Leu Pro Ser Leu Ile Lys Leu Asp Leu Ser Ser Asn
420 425 430

Leu Leu Ser Ser Phe Pro Ile Thr Gly Leu His Gly Leu Thr His Leu
435 440 445

Lys Leu Thr Gly Asn His Ala Leu Gln Ser Leu Ile Ser Ser Glu Asn
450 455 460

Phe Pro Glu Leu Lys Val Ile Glu Met Pro Tyr Ala Tyr Gln Cys Cys

465		470		475		480
Ala Phe Gly Val	Cys Glu Asn Ala Tyr Lys Ile Ser Asn Gln Trp Asn					
	485		490		495	
Lys Gly Asp Asn Ser Ser Met Asp Asp Leu His Lys Lys Asp Ala Gly						
	500		505		510	
Met Phe Gln Ala Gln Asp Glu Arg Asp Leu Glu Asp Phe Leu Leu Asp						
	515		520		525	
Phe Glu Glu Asp Leu Lys Ala Leu His Ser Val Gln Cys Ser Pro Ser						
	530		535		540	
Pro Gly Pro Phe Lys Pro Cys Glu His Leu Leu Asp Gly Trp Leu Ile						
	545		550		555	560
Arg Ile Gly Val Trp Thr Ile Ala Val Leu Ala Leu Thr Cys Asn Ala						
	565		570		575	
Leu Val Thr Ser Thr Val Phe Arg Ser Pro Leu Tyr Ile Ser Pro Ile						
	580		585		590	
Lys Leu Leu Ile Gly Val Ile Ala Ala Val Asn Met Leu Thr Gly Val						
	595		600		605	
Ser Ser Ala Val Leu Ala Gly Val Asp Ala Phe Thr Phe Gly Ser Phe						
	610		615		620	
Ala Arg His Gly Ala Trp Trp Glu Asn Gly Val Gly Cys His Val Ile						
	625		630		635	640
Gly Phe Leu Ser Ile Phe Ala Ser Glu Ser Ser Val Phe Leu Leu Thr						
	645		650		655	
Leu Ala Ala Leu Glu Arg Gly Phe Ser Val Lys Tyr Ser Ala Lys Phe						
	660		665		670	
Glu Thr Lys Ala Pro Phe Ser Ser Leu Lys Val Ile Ile Leu Leu Cys						
	675		680		685	
Ala Leu Leu Ala Leu Thr Met Ala Ala Val Pro Leu Leu Gly Gly Ser						
	690		695		700	

Lys Tyr Gly Ala Ser Pro Leu Cys Leu Pro Leu Pro Phe Gly Glu Pro
 705 710 715 720

Ser Thr Met Gly Tyr Met Val Ala Leu Ile Leu Leu Asn Ser Leu Cys
 725 730 735

Phe Leu Met Met Thr Ile Ala Tyr Thr Lys Leu Tyr Cys Asn Leu Asp
 740 745 750

Lys Gly Asp Leu Glu Asn Ile Trp Asp Cys Ser Met Val Lys His Ile
 755 760 765

Ala Leu Leu Leu Phe Thr Asn Cys Ile Leu Asn Cys Pro Val Ala Phe
 770 775 780

Leu Ser Phe Ser Ser Leu Ile Asn Leu Thr Phe Ile Ser Pro Glu Val
 785 790 795 800

Ile Lys Phe Ile Leu Leu Val Val Val Pro Leu Pro Ala Cys Leu Asn
 805 810 815

Pro Leu Leu Tyr Ile Leu Phe Asn Pro His Phe Lys Glu Asp Leu Val
 820 825 830

Ser Leu Arg Lys Gln Thr Tyr Val Trp Thr Arg Ser Lys His Pro Ser
 835 840 845

Leu Met Ser Ile Asn Ser Asp Asp Val Glu Lys Gln Ser Cys Asp Ser
 850 855 860

Thr Gln Ala Leu Val Thr Phe Thr Ser Ser Ser Ile Thr Tyr Asp Leu
 865 870 875 880

Pro Pro Ser Ser Val Pro Ser Pro Ala Tyr Pro Val Thr Glu Ser Cys
 885 890 895

His Leu Ser Ser Val Ala Phe Val Pro Cys Leu
 900 905

<210> 3
 <211> 828
 <212> PRT

<213> Homo sapiens

<400> 3

Met Arg Leu Glu Gly Glu Gly Arg Ser Ala Arg Ala Gly Gln Asn Leu
1 5 10 15

Ser Arg Ala Gly Ser Ala Arg Arg Gly Ala Pro Arg Asp Leu Ser Met
20 25 30

Asn Asn Leu Thr Glu Leu Gln Pro Gly Leu Phe His His Leu Arg Phe
35 40 45

Leu Glu Glu Leu Arg Leu Ser Gly Asn His Leu Ser His Ile Pro Gly
50 55 60

Gln Ala Phe Ser Gly Leu Tyr Ser Leu Lys Ile Leu Met Leu Gln Asn
65 70 75 80

Asn Gln Leu Gly Gly Ile Pro Ala Glu Ala Leu Trp Glu Leu Pro Ser
85 90 95

Leu Gln Ser Leu Asp Leu Asn Tyr Asn Lys Leu Gln Glu Phe Pro Val
100 105 110

Ala Ile Arg Thr Leu Gly Arg Leu Gln Glu Leu Gly Phe His Asn Asn
115 120 125

Asn Ile Lys Ala Ile Pro Glu Lys Ala Phe Met Gly Asn Pro Leu Leu
130 135 140

Gln Thr Ile His Phe Tyr Asp Asn Pro Ile Gln Phe Val Gly Arg Ser
145 150 155 160

Ala Phe Gln Tyr Leu Pro Lys Leu His Thr Leu Ser Leu Asn Gly Ala
165 170 175

Met Asp Ile Gln Glu Phe Pro Asp Leu Lys Gly Thr Thr Ser Leu Glu
180 185 190

Ile Leu Thr Leu Thr Arg Ala Gly Ile Arg Leu Leu Pro Ser Gly Met
195 200 205

Cys Gln Gln Leu Pro Arg Leu Arg Val Leu Glu Leu Ser His Asn Gln

210	215	220
Ile Glu Glu Leu Pro Ser Leu His Arg Cys Gln Lys Leu Glu Glu Ile		
225	230	235 240
Gly Leu Gln His Asn Arg Ile Trp Glu Ile Gly Ala Asp Thr Phe Ser		
	245	250 255
Gln Leu Ser Ser Leu Gln Ala Leu Asp Leu Ser Trp Asn Ala Ile Arg		
	260	265 270
Ser Ile His Pro Glu Ala Phe Ser Thr Leu His Ser Leu Val Lys Leu		
	275	280 285
Asp Leu Thr Asp Asn Gln Leu Thr Thr Leu Pro Leu Ala Gly Leu Gly		
	290	295 300
Gly Leu Met His Leu Lys Leu Lys Gly Asn Leu Ala Leu Ser Gln Ala		
305	310	315 320
Phe Ser Lys Asp Ser Phe Pro Lys Leu Arg Ile Leu Glu Val Pro Tyr		
	325	330 335
Ala Tyr Gln Cys Cys Pro Tyr Gly Met Cys Ala Ser Phe Phe Lys Ala		
	340	345 350
Ser Gly Gln Trp Glu Ala Glu Asp Leu His Leu Asp Asp Glu Glu Ser		
	355	360 365
Ser Lys Arg Pro Leu Gly Leu Leu Ala Arg Gln Ala Glu Asn His Tyr		
	370	375 380
Asp Gln Asp Leu Asp Glu Leu Gln Leu Glu Met Glu Asp Ser Lys Pro		
385	390	395 400
His Pro Ser Val Gln Cys Ser Pro Thr Pro Gly Pro Phe Lys Pro Cys		
	405	410 415
Glu Tyr Leu Phe Glu Ser Trp Gly Ile Arg Leu Ala Val Trp Ala Ile		
	420	425 430
Val Leu Leu Ser Val Leu Cys Asn Gly Leu Val Leu Leu Thr Val Phe		
	435	440 445

Ala Gly Gly Pro Val Pro Leu Pro Pro Val Lys Phe Val Val Gly Ala
 450 455 460

Ile Ala Gly Ala Asn Thr Leu Thr Gly Ile Ser Cys Gly Leu Leu Ala
 465 470 475 480

Ser Val Asp Ala Leu Thr Phe Gly Gln Phe Ser Glu Tyr Gly Ala Arg
 485 490 495

Trp Glu Thr Gly Leu Gly Cys Arg Ala Thr Gly Phe Leu Ala Val Leu
 500 505 510

Gly Ser Glu Ala Ser Val Leu Leu Leu Thr Leu Ala Ala Val Gln Cys
 515 520 525

Ser Val Ser Val Ser Cys Val Arg Ala Tyr Gly Lys Ser Pro Ser Leu
 530 535 540

Gly Ser Val Arg Ala Gly Val Leu Gly Cys Leu Ala Leu Ala Gly Leu
 545 550 555 560

Ala Ala Ala Leu Pro Leu Ala Ser Val Gly Glu Tyr Gly Ala Ser Pro
 565 570 575

Leu Cys Leu Pro Tyr Ala Pro Pro Glu Gly Gln Pro Ala Ala Leu Gly
 580 585 590

Phe Thr Val Ala Leu Val Met Met Asn Ser Phe Cys Phe Leu Val Val
 595 600 605

Ala Gly Ala Tyr Ile Lys Leu Tyr Cys Asp Leu Pro Arg Gly Asp Phe
 610 615 620

Glu Ala Val Trp Asp Cys Ala Met Val Arg His Val Ala Trp Leu Ile
 625 630 635 640

Phe Ala Asp Gly Leu Leu Tyr Cys Pro Val Ala Phe Leu Ser Phe Ala
 645 650 655

Ser Met Leu Gly Leu Phe Pro Val Thr Pro Glu Ala Val Lys Ser Val
 660 665 670

Leu Leu Val Val Leu Pro Leu Pro Ala Cys Leu Asn Pro Leu Leu Tyr
675 680 685

Leu Leu Phe Asn Pro His Phe Arg Asp Asp Leu Arg Arg Leu Arg Pro
690 695 700

Arg Ala Gly Asp Ser Gly Pro Leu Ala Tyr Ala Ala Ala Gly Glu Leu
705 710 715 720

Glu Lys Ser Ser Cys Asp Ser Thr Gln Ala Leu Val Ala Phe Ser Asp
725 730 735

Val Asp Leu Ile Leu Glu Ala Ser Glu Ala Gly Arg Pro Pro Gly Leu
740 745 750

Glu Thr Tyr Gly Phe Pro Ser Val Thr Leu Ile Ser Cys Gln Gln Pro
755 760 765

Gly Ala Pro Arg Leu Glu Gly Ser His Cys Val Glu Pro Glu Gly Asn
770 775 780

His Phe Gly Asn Pro Gln Pro Ser Met Asp Gly Glu Leu Leu Leu Arg
785 790 795 800

Ala Glu Gly Ser Thr Pro Ala Gly Gly Gly Leu Ser Gly Gly Gly Gly
805 810 815

Phe Gln Pro Ser Gly Leu Ala Phe Ala Ser His Val
820 825

<210> 4
<211> 955
<212> PRT
<213> Homo sapiens

<400> 4

Met Pro Gly Pro Leu Gly Leu Leu Cys Phe Leu Ala Leu Gly Leu Leu
1 5 10 15

Gly Ser Ala Gly Pro Ser Gly Ala Ala Pro Pro Leu Cys Ala Ala Pro
20 25 30

Cys Ser Cys Asp Gly Asp Arg Arg Val Asp Cys Ser Gly Lys Gly Leu

35	40	45													
Thr	Ala	Val	Pro	Glu	Gly	Leu	Ser	Ala	Phe	Thr	Gln	Ala	Leu	Asp	Ile
50						55					60				
Ser	Met	Asn	Asn	Ile	Thr	Gln	Leu	Pro	Glu	Asp	Ala	Phe	Lys	Asn	Phe
65					70					75					80
Pro	Phe	Leu	Glu	Glu	Leu	Gln	Leu	Ala	Gly	Asn	Asp	Leu	Ser	Phe	Ile
				85					90					95	
His	Pro	Lys	Ala	Leu	Ser	Gly	Leu	Lys	Glu	Leu	Lys	Val	Leu	Thr	Leu
			100					105					110		
Gln	Asn	Asn	Gln	Leu	Lys	Thr	Val	Pro	Ser	Glu	Ala	Ile	Arg	Gly	Leu
			115				120						125		
Ser	Ala	Leu	Gln	Ser	Leu	Arg	Leu	Asp	Ala	Asn	His	Ile	Thr	Ser	Val
	130					135					140				
Pro	Glu	Asp	Ser	Phe	Glu	Gly	Leu	Val	Gln	Leu	Arg	His	Leu	Trp	Leu
145					150					155					160
Asp	Asp	Asn	Ser	Leu	Thr	Glu	Val	Pro	Val	His	Pro	Leu	Ser	Asn	Leu
				165					170					175	
Pro	Thr	Leu	Gln	Ala	Leu	Thr	Leu	Ala	Leu	Asn	Lys	Ile	Ser	Ser	Ile
			180					185					190		
Pro	Asp	Phe	Ala	Phe	Thr	Asn	Leu	Ser	Ser	Leu	Val	Val	Leu	His	Leu
	195						200					205			
His	Asn	Asn	Lys	Ile	Arg	Ser	Leu	Ser	Gln	His	Cys	Phe	Asp	Gly	Leu
	210					215					220				
Asp	Asn	Leu	Glu	Thr	Leu	Asp	Leu	Asn	Tyr	Asn	Asn	Leu	Gly	Glu	Phe
225					230					235					240
Pro	Gln	Ala	Ile	Lys	Ala	Leu	Pro	Ser	Leu	Lys	Glu	Leu	Gly	Phe	His
				245					250					255	
Ser	Asn	Ser	Ile	Ser	Val	Ile	Pro	Asp	Gly	Ala	Phe	Asp	Gly	Asn	Pro
			260					265					270		

Leu Leu Arg Thr Ile His Leu Tyr Asp Asn Pro Leu Ser Phe Val Gly
 275 280 285

Asn Ser Ala Phe His Asn Leu Ser Asp Leu His Ser Leu Val Ile Arg
 290 295 300

Gly Ala Ser Met Val Gln Gln Phe Pro Asn Leu Thr Gly Thr Val His
 305 310 315 320

Leu Glu Ser Leu Thr Leu Thr Gly Thr Lys Ile Ser Ser Ile Pro Asn
 325 330 335

Asn Leu Cys Gln Glu Gln Lys Met Leu Arg Thr Leu Asp Leu Ser Tyr
 340 345 350

Asn Asn Ile Arg Asp Leu Pro Ser Phe Asn Gly Cys His Ala Leu Glu
 355 360 365

Glu Ile Ser Leu Gln Arg Asn Gln Ile Tyr Gln Ile Lys Glu Gly Thr
 370 375 380

Phe Gln Gly Leu Ile Ser Leu Arg Ile Leu Asp Leu Ser Arg Asn Leu
 385 390 395 400

Ile His Glu Ile His Ser Arg Ala Phe Ala Thr Leu Gly Pro Ile Thr
 405 410 415

Asn Leu Asp Val Ser Phe Asn Glu Leu Thr Ser Phe Pro Thr Glu Gly
 420 425 430

Leu Asn Gly Leu Asn Gln Leu Lys Leu Val Gly Asn Phe Lys Leu Lys
 435 440 445

Glu Ala Leu Ala Ala Lys Asp Phe Val Asn Leu Arg Ser Leu Ser Val
 450 455 460

Pro Tyr Ala Tyr Gln Cys Cys Ala Phe Trp Gly Cys Asp Ser Tyr Ala
 465 470 475 480

Asn Leu Asn Thr Glu Asp Asn Ser Leu Gln Asp His Ser Val Ala Gln
 485 490 495

Glu Lys Gly Lys Cys Met Ser Thr Ala Asp Ala Ala Asn Val Thr Ser
 500 505 510

Thr Leu Glu Asn Glu Glu His Ser Gln Ile Ile Ile His Cys Thr Pro
 515 520 525

Ser Thr Gly Ala Phe Lys Pro Cys Glu Tyr Leu Leu Gly Ser Trp Met
 530 535 540

Ile Arg Leu Thr Val Trp Phe Ile Phe Leu Val Ala Leu Phe Phe Asn
 545 550 555 560

Leu Leu Val Ile Leu Thr Thr Phe Ala Ser Cys Thr Ser Leu Pro Ser
 565 570 575

Ser Lys Leu Phe Ile Gly Leu Ile Ser Val Ser Asn Leu Phe Met Gly
 580 585 590

Ile Tyr Thr Gly Ile Leu Thr Phe Leu Asp Ala Val Ser Trp Gly Arg
 595 600 605

Phe Ala Glu Phe Gly Ile Trp Trp Glu Thr Gly Ser Gly Cys Lys Val
 610 615 620

Ala Gly Phe Leu Ala Val Phe Ser Ser Glu Ser Ala Ile Phe Leu Leu
 625 630 635 640

Met Leu Ala Thr Val Glu Arg Ser Leu Ser Ala Lys Asp Ile Met Lys
 645 650 655

Asn Gly Lys Ser Asn His Leu Lys Gln Phe Arg Val Ala Ala Leu Leu
 660 665 670

Ala Phe Leu Gly Ala Thr Val Ala Gly Cys Phe Pro Leu Phe His Arg
 675 680 685

Gly Glu Tyr Ser Ala Ser Pro Leu Cys Leu Pro Phe Pro Thr Gly Glu
 690 695 700

Thr Pro Ser Leu Gly Phe Thr Val Thr Leu Val Leu Leu Asn Ser Leu
 705 710 715 720

Ala Phe Leu Leu Met Ala Val Ile Tyr Thr Lys Leu Tyr Cys Asn Leu
 725 730 735

Glu Lys Glu Asp Leu Ser Glu Asn Ser Gln Ser Ser Met Ile Lys His
 740 745 750

Val Ala Trp Leu Ile Phe Thr Asn Cys Ile Phe Phe Cys Pro Val Ala
 755 760 765

Phe Phe Ser Phe Ala Pro Leu Ile Thr Ala Ile Ser Ile Ser Pro Glu
 770 775 780

Ile Met Lys Ser Val Thr Leu Ile Phe Phe Pro Leu Pro Ala Cys Leu
 785 790 795 800

Asn Pro Val Leu Tyr Val Phe Phe Asn Pro Lys Phe Lys Glu Asp Trp
 805 810 815

Lys Leu Leu Lys Arg Arg Val Thr Lys Lys Ser Gly Ser Val Ser Val
 820 825 830

Ser Ile Ser Ser Gln Gly Gly Cys Leu Glu Gln Asp Phe Tyr Tyr Asp
 835 840 845

Cys Gly Met Tyr Ser His Leu Gln Gly Asn Leu Thr Val Cys Asp Cys
 850 855 860

Cys Glu Ser Phe Leu Leu Thr Lys Pro Val Ser Cys Lys His Leu Ile
 865 870 875 880

Lys Ser His Ser Cys Pro Ala Leu Ala Val Ala Ser Cys Gln Arg Pro
 885 890 895

Glu Gly Tyr Trp Ser Asp Cys Gly Thr Gln Ser Ala His Ser Asp Tyr
 900 905 910

Ala Asp Glu Glu Asp Ser Phe Val Ser Asp Ser Ser Asp Gln Val Gln
 915 920 925

Ala Cys Gly Arg Ala Cys Phe Tyr Gln Ser Arg Gly Phe Pro Leu Val
 930 935 940

Arg Tyr Ala Tyr Asn Leu Pro Arg Val Lys Asp

945

950

955